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Thomas-Fermi calculation of bilayer interaction in phospholipid membrane

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A calculation for bilayer interaction in phospholipid membrane is performed using the Thomas-Fermi statistical method in which Dirac's exchange and the quantum corrections are treated as perturbations It has been shown that the method is able to explain satisfactorily the stability of a phospholipid bilayer. The binding energy and the force constant of the lipid bilayer are obtained. The calculated binding energy gives rise to a value for the equilibrium membrane thickness in good agreement with the experimental datum

1. INTRODUCTION

Membrane lipids are mostly phospholipids (figure 1). A phospholipid molecule has a hydrophilic part at its one end and the remainder is hydrophobic. The bulk of the membrane lipids are in a bilayer resulting from combined effects of hydrophobic and hydrophilic interactions and it is the most stable configuration. Paramagnetic resonance spectroscopic studies (McConnell & McFarland 1972) have revealed a flexibility gradient along the length of a lipid molecule There is a high frequency anisotropic motion of the molecule fixed axis system (x, y, z) about an *average* axis system (x', y', z'). The *average* axis system has an axially symmetric distribution about the normal N to the bilayer surface. As the number of CH_2 units in a phospholipid molecule increases, the average principal axis direction z' becomes more and more parallel to N (Gaffney & McConnell 1974). So our analysis of bilayer interaction in a phospholipid membrane assumes that this *average* principal axis direction z' is parallel to N.

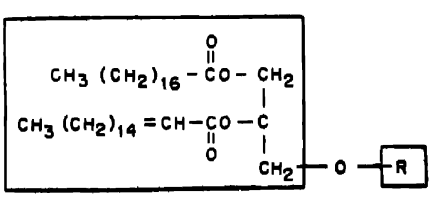

Fig. 1. General structure of a phospholipid molecule.

The interaction between one layer of phospholipids with that of the other in a bilayer membrane has been studied here using the Thomas-Fermi (T.F.) statistical method The study of this interaction is very important in understanding the stability and other physical features of the membrane. In the present formulation we assume that only a small part of the hydrocarbon chain near the free edge of the molecule is involved in the bilayer interaction and contribution of the rest of the molecule is negligible. We simplify the problem by first quenching the interacting part of each lipid molecule to a point nucleus of charge Ze surrounded by Z electrons, where Ze is the total nuclear charge of the interacting part of a molecule. These hypothetical point nuclei in each layer are arranged in a body—centred hexagonal lattice which is the distribution of polar parts of lipid molecules in a single layer We then substitute homogeneous planar distribution of electric charge for each such layered distribution of hypothetical nuclei. We then calculate the interlayer force as well as binding energy of the membrane.

2. Method of Calculation

The proposed formulation simplifies the TF equation in Hartree's atomic unit ($\hbar = m = e = 1$) to

$$\frac{d^2\phi}{dx^2} = \frac{8\sqrt{2}}{3\pi}\,\phi^{3/2}, \qquad \ldots (1)$$

where ϕ is the TF potential at a distance x from the nearest layer. We take the TF equation as our starting equation and the exchange and quantum corrections to TF energy formula as perturbations The boundary conditions are

$$E(x = 0) = E_0 \quad \text{and} \quad E(x = R/2) = 0, \qquad \ldots (2)$$

where $E = -d\phi/dx$, R is the separation between the hypothetical layers and $E_0 = 2\pi\sigma$, where σ is the charge per unit area of a single layer and is given by

$$\sigma = \frac{2Z}{\sqrt{3}d^2} \qquad \ldots (3)$$

Here d is the distance between two nearest hypothetical nuclei in a layer. d is obtained from the knowledge of the surface available to a polar part of lipid molecule which is about 40 Å^2 (Luzzati). Then

$$4\pi\, d^2/4 = 40 \text{ Å}^2$$

i.e., $d = 6.735$ a.u.

Taking four hydrocarbon atomic groups of each fatty acid chain of the lipid molecule as interacting, Z becomes 66 so that $E_0 = 9.606$ a.u.

Following Santos & Villagra (1972) we solve eq. (1) to find

$$R = 2\left(\frac{9\pi^2}{250}\right)^{1/5}\int_0^{E_0}(E^2+C)^{-3/5}dE, \qquad \ldots (4)$$

where C is a constant of integration. We also find the TF energy U_{TF} and Dirac's exchange correction U_D and Kirznit's quantum correction U_K to U_{TF} as

$$U_{TF} = \frac{A}{288\pi}\left[(60\pi)^{2/5}\{5E_0(E_0^2+C)^{2/5} - 5E_0^{9/5}\} + 2CR\right], \qquad \ldots (5)$$

$$U_D = -\frac{3A}{224\pi^2}[60\pi]^{1/5}\left[2C\int_0^{E_0}(E^2+C)^{-4/5}dE + 5E_0(E_0^2+C)^{1/5} - 5E_0^{7/5}\right], \quad \ldots (6)$$

$$U_K = \frac{A}{28\pi^2}(60\pi)^{1/5}\left[E_0^{7/5} - E_0(E_0^2+C)^{1/5} - \frac{1}{6}C\int_0^{E_0}(E^2+C)^{-4/5}dE\right], \qquad \ldots (7)$$

where A is the area of a hypothetical layer whose charge is $Z = 66$ a.u. This area is so chosen that there are on the average 66 electrons in a volume $\frac{1}{2}AR$, which gives $A = 43.17$ a.u

The integrals in eqs. (4), (6) and (7) are expanded in convergent series

$$\int_0^{E_0}(E^2+C)^{-3/5}dE = 5.6606C^{-1/10} + E_0^{-1/5}\left[5 - \frac{3}{11}\alpha + \frac{12}{105}\alpha^2 - \frac{52}{775}\alpha^3 + 0(\alpha^4)\right],$$

and $\qquad \ldots (8)$

$$\int_0^{E_0}(E^2+C)^{-4/5}dE = 2.2772C^{-3/10} - E_0^{-3/5}\left[\frac{5}{3} - \frac{4}{13}\alpha + \frac{18}{105}\alpha^2 - \frac{84}{825}\alpha^3 + 0(\alpha^4)\right],$$

for $\alpha = \dfrac{C}{E_0^2} < 1.$ $\qquad \ldots (9)$

3. Results and Discussion

Values of U_{TF}, $U_{TF}+D_D$ and $U_{TF}+U_D+U_K$ are obtained for different values of the separation R between the hypothetical layers. The results are shown in figure 2. It is found that while the TF theory does not give rise to any binding of the phospholipid bilayer, the TFD theories without and with quantum corrections do. The binding energy of the hypothetical bilayer for its equilibrium configuration corresponds to the minimum of the function $U(R)$ and the force constant to the second derivative of this function at the minimum. The binding energy and the force constant of the actual phospholipid bilayer are those obtained for the hypothetical bilayer. The results are shown is table 1.

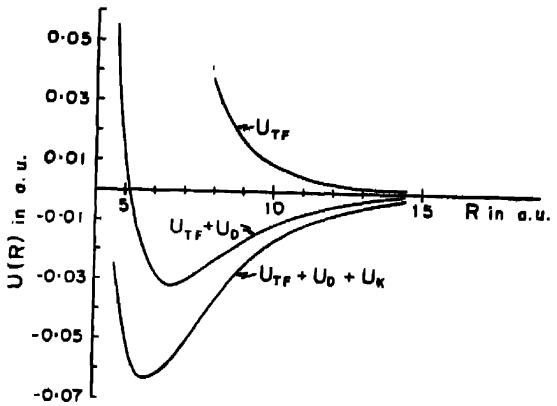

Fig. 2. Variation of U_{TF}, $U_{TF}+U_D$ and $U_{TF}+D_D+U_K$ with R.

Table 1

	Binding Energy	Force Constant
Calculated from $U_{TF}+U_D$	0 032 a.u.	0.028 a.u.
Calculated from $U_{TF}+U_D+U_R$	0.064 a.u.	0.062 a.u.

An approximate check on our result can be had by a calculation of the membrane thickness for its equilibrium configuration from the value of its binding energy. The form of the hydrocarbon chain of a phospholipid molecule may be characterised solely by the specification of the straight line distance l between the ends (figure 3). The beginning A of the chain is held fast to the polar part of the lipid molecule concerned. The free edge B of the hycrocarbon chain is subject to a

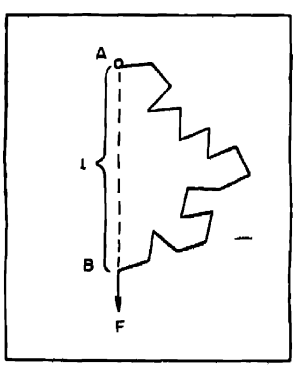

Fig. 3. Schematic representation of the configuration of a lipid molecule in phospholipid bilayer.

force F provided by the bilayer interaction and this force is in the direction AB perpendicular to the bilayer surface. The equilibrium length corresponding to the tension F may be given approximately by the formula (Joos),

$$F = \frac{3kTl}{Na^2}, \qquad \ldots (10)$$

where k is Boltzmann's constant, T the temperature, N the number of C–C units and a the length of each such unit. The potential energy of a hydrocarbon chain in equilibrium in a phospholipid bilayer is

$$Fl = \frac{3kTl^2}{Na^2} \qquad \ldots (11)$$

which is also the binding energy per lipid molecule in the membrane bilayer. Taking $a = 1.53$ Å, $T = 273°K$ and $N \sim 20$, and using the value for the binding energy per molecule obtained from the TF DK calculation, we have $l = 48.08$ a.u. The equilibrium membrane thickness may be approximately given by

$$S = 2(l+d), \qquad \ldots (12)$$

where d is 6.735 a.u. as found earlier. The result is shown in table 2, which shows that the agreement between the calculated and experimental values for membrane thickness is reasonably good. The calculated result is expected to be higher than the observed one as there may be some penetration of fatty acid chains of lipid molecules of one layer into the other.

Table 2

	Experimental (Vandev Kooi, 1972)	Calculated
Membrane thickness	85.06 a.u.	109.63 a.u.

The present report attempts to understand the nature of lipid-lipid interaction, providing some quantitative information about the interlayer force and the binding energy of the two lipid layers in a membrane. Although our calculation considers four hydrocarbon atomic groups of each fatty acid chain of a phospholipid molecule as involved in bilayer interaction in a membrane, a similar consideration of a few more or less hydrocarbon atomic groups, with the condition that the interacting part of a hydrocarbon chain is small, will not change the essence of our results substantially.

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